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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
10/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/583,188	GORDON ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30 and 33-42* is/are pending in the application.

4a) Of the above claim(s) *23-25 and 33-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of the invention of Group I, drawn to an isolated stem cell population, in the reply filed on 06/09/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). In the same reply, Applicant elected the species of "inhibitory RNA sequence". However, upon further consideration, the species election requirement is hereby withdrawn.

Claims 31 and 32 have been cancelled. Claims 2-16, 20-22, 26-28, and 30 have been amended.

Claims 23-25 and 33-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim.

Claims 1-22 and 26-30 are under examination.

Specification

2. The use of the trademarks Resovist, MiniMacs, and Lymphoprep has been noted in this application (p. 16, 19, 21, 22, and 25). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, 2nd paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting how the stem cells isolation is performed.

Claim Rejections - 35 USC § 112, 1st paragraph – Biological Deposit

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure meets the

enablement requirement of 35 USC § 112, first paragraph, have been described by the court in *In re Wands,* 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skills of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided.

Claims 1 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabling without either complete evidence that the cells deposited with ECACC recited in the claims are known and **readily available to the public** or complete evidence of the deposit of the biological material. Because the biological material is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological material is not so obtainable or available, the requirements of 35 USC §112 may be satisfied by a deposit of the biological materials. It is not apparent from the disclosure if the biological materials are readily available to the public. On p. 8, lines 14-18, the specification refers to the cells, but does not state that all restrictions on the deposits will be irrevocably removed on issuance of a patent. In the absence of

evidence showing that the cells are publicly available (i.e., deposited in compliance with 37 CFR 1.801-1.809), claims 1 and 11 are not supported by an enabling disclosure.

A suitable deposit for patent purposes would overcome this ground of rejection. Deposits should be made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. The Examiner notes that, if Applicant argues that the cells deposited with the accession no. 04092401 are well known and readily available to the public, the claims drawn in part to these cells will only remain enforceable while the cells remain readily available to the public. If the deposit has not been made under the Budapest Treaty, then in order to

certify that the deposit meets the criteria set forth in 37 CFR §§1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability o the biological material at the time of deposit will be made (see 37 CR §1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to MPEP §2400 in general, and specifically to §2144.05, as well as to 37 CFR §1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-9, 12, 13, 16, 18, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Young et al. (The Anatomical Record, 2001, 264: 51-62).

Young et al. teach obtaining an isolated stem cell population capable of adhering to tissue culture plastic plates and capable of being cultivated in the absence of a feeder layer, wherein the stem cells are adult human stem cells derived from connective tissue, wherein the stem cell population has the phenotype $CD34^+$ $Thy\text{-}1^+$ $CD33^-$ $CD38^-$ $HLA\text{-}DR^-$ $CD3^-$, and wherein the stem cell population is capable of surviving cryopreservation (claims 1, 3, 4, 9, 12, 13, 16, 18, and 27) (Abstract, p. 52, column 2, p. 59, column 2, first full paragraph). With respect to the capability to differentiate into cells of ectodermal, mesodermal, or endodermal origin (claims 1 and 18), capability to adhere within 3 h and remain adherent for at least 72 h (claim 2), absence of CD19 expression (claim 3), or the expressed genes recited in claims 5 and 6, it is noted that as claimed and as disclosed in the specification, all that is required for a cell to exhibit such properties is to adhere to plastic and express CD34 ; since the stem cell population of Young et al. expresses CD34 and adheres to plastic, it must necessarily be negative for CD19 and positive for the genes recited in claims 5 and 6, capable of differentiation into ectodermal, mesodermal, or endodermal cells, capable of adhering within 3 h, and capable of remaining adherent for at least 72 h. Moreover, since the stem cell

population of Young et al. is capable of differentiating into ectodermal, mesodermal, or endodermal cells, it must necessarily give rise to progeny expressing genes as recited in claims 7 and 8, which genes are differentiation markers for cells of ectodermal, mesodermal, or endodermal origin. Since Young et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

9. Claims 1-9, 12, 13, 16-22, 26, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Gordon et al. (Leukemia, 1996, 10: 1347-1353), as evidenced by Ferrero et al. (Bone Marrow Transplantation, 1908, 21: 409-413).

Gordon et al. teach an isolated adult human stem cell population and a method of obtaining the population, wherein the method comprises subjecting bone marrow cells to Lymphoprep density gradient separation, collecting the cells and isolating the CD34-expressing cells by using magnetic beads coated with anti-CD34 antibodies, recovering the attached CD34-expressing cells, plating the cells on a tissue culture plastic dish, followed by the recovery of the adherent cells and their further cultivation without a feeder layer (claims 1, 9, 12, 13, 16, 17, 19-22, 26) (Abstract, p. 1347, column 2, last paragraph, p. 1348, columns 1 and 2, p. 1349, column 2). Although Gordon et al. do not specifically teach collecting the low density cells (step (ii) in claims 17 and 20), they must necessarily do so because the use Lymphoprep density gradient centrifugation results in the recovery of CD34-positive cells in the low density fraction (see Ferrero et al., p. 410, column 2). With respect to the capability to differentiate into cells of ectodermal, mesodermal, or endodermal origin (claims 1 and 17-19), capability

to adhere within 3 h and remain adherent for at least 72 h (claim 2), to exhibit the phenotype recited in claims 3-6, or to survive cryopreservation (claim 27), it is noted that as claimed and as disclosed in the specification, all that is required for a cell to exhibit such properties is to adhere to plastic and express CD34; since the stem cell population of Gordon et al. expresses CD34 and adheres to plastic, it must necessarily exhibit all these properties. Moreover, since the stem cell population of Young et al. is capable of differentiating into ectodermal, mesodermal, or endodermal cells, it must necessarily give rise to progeny expressing genes as recited in claims 7 and 8, which genes are differentiation markers for cells of ectodermal, mesodermal, or endodermal origin. Since Gordon et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-10, 12-22, and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon et al. taken with Ferrero et al., Sugiura et al. (Blood, 1992, 80: 1463-1469), and Wagner et al. (U.S. Patent No. 5,807,686).

The teachings of Gordon et al. and Ferrero et al. are applied as above for claims 1-9, 12, 13, 16-22, 26, and 27. Gordon et al. and Ferrero et al. do not specifically teach

obtaining their cell population from umbilical cord (claim 10), nor do they teach genetically modifying their cells (claims 28-30). However, the prior art teaches that, similar to bone marrow, umbilical cord contains $CD34^+$ plastic-adherent stem cells (see Sugiura et al., p. 1463, column 2). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the teachings of Gordon et al. and Ferrero et al. by substituting their bone marrow with umbilical cord blood to achieve the predictable result of obtaining an adhering stem cell population capable of differentiating into ectodermal, mesodermal, or endodermal cells (claim 10). Gordon et al., Ferrero et al., and Sugiura et al. do not teach genetically modifying the cells. Wagner et al. teach genetically modifying the cells $CD34^+$ cells by retroviral infection, wherein such cells are suitable for transplantation (claims 28 and 29) (column 3, lines 64-67, column 4, lines 1-8). Based on these teachings, it would have obvious to one of skill in the art, at the time the invention was made, to modify the cells of Gordon et al., Ferrero et al., and Sugiura et al. according to the teachings of Wagner et al. to achieve the predictable result of obtaining cells suitable of being transplanted into subjects to correct genetic defects. With respect to the limitation recited in claim 30, it would have been within the knowledge and abilities of one of skill in the art to use an antisense oligonucleotide when studying the role of specific genes in proliferation or differentiation. With respect to the limitation recited in claims 14 and 15, one of skill in the art would have known to isolate such cells when stem cell transplantation in horses or companion animals was needed. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD
/Ileana Popa/
Examiner, Art Unit 1633